CASE REPORT

Mycobacterium-associated Lobular Panniculitis, Mimicking a Rheumatoid Nodule in a Patient With Rheumatoid Arthritis

*Wei-Sheng Chen,[1] Yu-Fen Lee,[2] Hon-Pin Wang,[1] Kuei-Ying Su,[1,3] Cheng-Hon Lee,[1] De-Feng Huang[1,4]**

Mycobacterium-associated lobular panniculitis can mimic a rheumatoid nodule and has been seldom reported in rheumatoid arthritis (RA). We describe a 69-year-old woman with RA who presented initially with fever and an indurated skin lesion on the right thigh. Lobular panniculitis was diagnosed after biopsy and was then treated with prednisolone. After this therapy, pulmonary infiltration developed and was later shown by transbronchial biopsy to be caused by *Mycobacterium tuberculosis*. The panniculitis skin lesion became smaller after prednisolone therapy and was further improved after antituberculosis drugs were added. Reexamination of the previously biopsied skin tissue disclosed acid-fast bacilli. Reactivation or new infection of *M. tuberculosis* is a current important issue in RA patients, especially after treatment with disease-modifying anti-rheumatic drugs or antitumor necrosis factor agents. *Mycobacterium*-associated lobular panniculitis should be included in the differential diagnosis of indurated skin disorder in RA patients, and acid-fast staining or polymerase chain reaction examination of tuberculosis should be performed routinely on biopsied skin tissue. [*J Formos Med Assoc* 2009;108(8):673–676]

Key Words: panniculitis, rheumatoid arthritis, rheumatoid nodule, tuberculosis

Panniculitis is an inflammatory subcutaneous fat disorder that has many possible etiologies, such as drugs, autoimmune diseases, malignancy, trauma, or infections. The most common infectious agents associated with this disorder include streptococci, *Mycobacterium* and *Mycoplasma pneumoniae*. Rheumatoid arthritis (RA) is a systemic disease that is characterized by the presence of symmetrical polyarthritis and extra-articular organ/system involvement in severe cases. Rheumatoid nodules are one of the major extra-articular cutaneous manifestations in RA, and are present usually on the extensor sides of the four limbs. Occasionally, they can be atypically manifested as linear, papular and ulcerative lesions.[1] Lobar panniculitis—that presents as a nodular-like skin lesion—has been seldom reported in RA. Here, we report an RA patient who presented with fever and a nodular skin lesion on the extensor side of the right thigh. The skin lesion was initially thought to be a rheumatoid nodule, but was finally demonstrated to be *Mycobacterium*-associated lobular panniculitis.

[1]Division of Allergy, Immunology, and Rheumatology, Department of Medicine, and [2]Department of Dermatology, Taipei Veterans General Hospital, and [4]Department of Medicine, National Yang-Ming University, Taipei; [3]Buddhist Tzu Chi General Hospital, Hualien, Taiwan.

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***Correspondence to:** Dr De-Feng Huang, Division of Allergy, Immunology, and Rheumatology, Department of Medicine, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan.
E-mail: dfhuang@vghtpe.gov.tw

Figure 1. A subcutaneous nodular induration developed on the right thigh of a patient with rheumatoid arthritis.

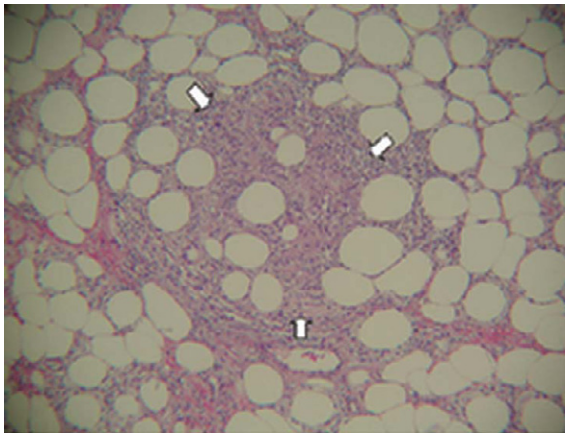

Figure 2. Histopathological studies from the indurated lesion of the right thigh revealed the changes of lobular panniculitis with mixed infiltrates of lymphohistiocytes and neutrophils in the fat lobules. (Hematoxylin & eosin; original magnification, 100×.)

Case Report

A 69-year-old woman with seropositive RA was admitted to Taipei Veterans General Hospital in September 2006 because of intermittent fever of up to 38.5°C, and an indurated, nodular-like skin lesion on the right thigh of 20 days' duration (Figure 1). Her RA had lasted for 10 years, with both hands severely affected, as shown by severe subluxation of metacarpopharyngeal (MCP) joints and numerous bony erosions in the MCP, proximal interphalangeal, and wrist joints. She had not received any disease-modifying antirheumatic drugs (DMARDs) in the previous 2 years. After admission, chest X-ray disclosed mild cardiomegaly, but was otherwise unremarkable. Complete blood count and a blood chemistry panel of liver and renal function tests were within normal limits, except for a moderate iron-deficiency anemia (hemoglobin, 8.3 mg/dL) and mild elevation of serum lactate dehydrogenase (407 μL/L; normal, < 213 μL/L). Erythrocyte sedimentation rate was elevated (77 mm/hour). Serum autoantibody profiles for systemic lupus erythematosus and antiphospholipid syndrome were negative, as were the infection surveys, including blood culture, hepatitis B and C viruses, syphilis, and leprosy. She was negative for the tumor markers α-fetoprotein, carcinoembryonic antigen, cancer antigen-153 and cancer antigen-199. Serum immunoelectrophoresis studies were unremarkable, although serum IgG level was reduced and IgA was increased slightly (IgG, 679 mg/dL; IgA, 563 mg/dL; IgM, 77 mg/dL; normal values: 751–1560 mg/dL, 82–453 mg/dL, and 46–304 mg/dL, respectively).

After admission, the antibiotic oxacillin (2 g every 6 hours) was given but discontinued 1 week later after fever subsided. Skin biopsy was performed on day 2 of admission and revealed the changes of lobular panniculitis with vasculitis, which consisted of subcutaneous focal fatty necrosis with lobular infiltration by lymphohistiocytes and neutrophils. In addition, fibrinoid necrosis with mild lymphocytic infiltration in some small vessels was noted (Figures 2 and 3). Prednisolone (15 mg/day) was thus administered from day 7 of admission, and the indurated erythematous skin lesion on the right thigh gradually became smaller thereafter. On day 23 of admission, dyspnea ensued and fever (38.5°C) recurred. New pulmonary infiltrations in both upper lung fields appeared on chest X-ray, and computed-tomography-guided lung biopsy disclosed granulomatous and inflammatory changes, with mycobacterial infection, as demonstrated by the presence of acid-fast bacilli. To determine the etiology of the skin lesion of the right thigh,

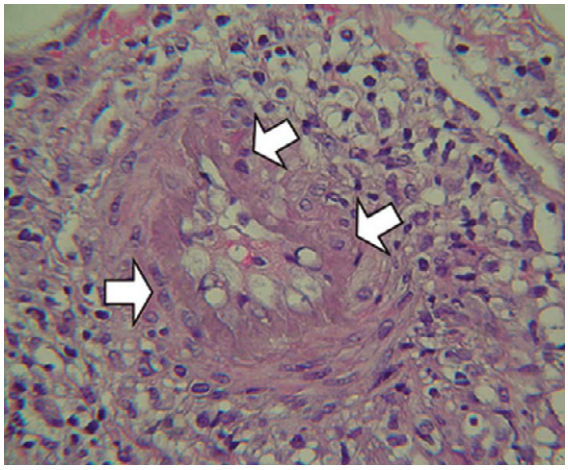

Figure 3. Histopathological studies from the indurated lesion of the right thigh disclosed fibrinoid necrosis with mild lymphocytic infiltration in the small vessels. (Hematoxylin & eosin; original magnification, 400×.)

we reexamined the previously biopsied skin tissue, in which acid-fast bacilli were found, although the polymerase chain reaction (PCR) for *M. tuberculosis* was negative. After 3 weeks of antituberculous drug therapy (isoniazid, ethambutol and rifampicin), fever subsided, pulmonary infiltrations improved, and the indurated skin rash decreased continually in size. During admission, no DMARDs were given for our patient's arthritis and skin disorder.

Discussion

Rheumatoid nodules are an important indicator for RA disease activity, and are one of the major cutaneous manifestations of RA.[2–4] The classical type, more frequently found and familiar to most physicians, is located usually on the extensor side of the forearm, lower limbs or buttocks, and is characterized pathologically by necrobiotic tissue surrounded by histiocytes or giant cells. Three variants of rheumatoid nodule have been described: (1) linear, papular and ulcerative type; (2) rheumatoid nodulosis; and (3) palindromic or recurrent rheumatism.[1] In the first variant, the nodule is often associated with vasculitis or ulceration. This variant is rarely described and only skin biopsy can prove the diagnosis. In view of its indurated nature, the skin lesion in our patient was considered initially as a variant type of rheumatoid nodule, but was finally shown to be *Mycobacterium*-associated lobular panniculitis.

Lobular panniculitis can be classified into two major categories, based on whether or not vasculitis is found.[5] The first category, panniculitis without vasculitis, includes sclerosing panniculitis, lupus panniculitis, pancreatitis panniculitis, classical rheumatoid nodule, and cold panniculitis; the second, panniculitis associated with vasculitis, as in the current report, comprises erythema nodosum leprosum, RA-associated neutrophilic lobular panniculitis, and erythema induratum. RA-associated neutrophilic lobular panniculitis can present clinically as a rheumatoid-nodule-like lesion and has been previously reported in a few RA patients.[6,7] This lesion is characterized pathologically by the appearance of severe adiposity necrosis in the fat lobule, in which neutrophils accompanied by histiocytes or giant cells are infiltrated—on occasion, leukocytoclastic vasculitis is observed.[8] Erythema nodosum leprosum is usually seen in patients with lepromatous leprosy who are undergoing sulfone therapy. Its clinical manifestations include tender erythematous nodular skin lesions, fever, myalgia, hepatosplenomegaly, neuritis orchitis, and glomerulonephritis. The major pathological findings are immune-complex-associated cutaneous vasculitis or neuritis.[9] Our patient did not have the above clinical and pathological findings, so erythema nodosum leprosy and RA-associated neutrophilic lobular panniculitis were excluded.

Tender red nodules with lobular panniculitis in the lower extremities are the typical changes of erythema induratum.[10] In the early stage of erythema induratum, fat lobules may be extensively necrotic, but are only infiltrated minimally by inflammatory cells, mostly neutrophils. In the more advanced stage, necrotic adipocytes can induce histiocytes to ingest lipids and become foamy in appearance. Granulomas infiltrated with giant cells and lymphocytes may appear. When intense vascular damage is present, tissue necrosis may extend to the overlying dermis and epidermis,

with ulceration and discharge of liquefied necrotic fat. Erythema induratum is thought to be an immune-mediated skin lesion that is reactive to some microorganisms. Recent studies have shown that *M. tuberculosis* is one of the major etiologic factors.[11,12] In a study based in Taiwan by Chen et al,[11] in which skin-biopsy tissue was reexamined by PCR, nine out of 12 cases of erythema induratum were later proven to be associated with *M. tuberculosis*. Mycobacterial infection is common in Taiwan. Skin nodules found in patients with RA can be mistaken easily as rheumatoid nodules, and therefore be treated aggressively with immunosuppressive drugs if no skin biopsy is performed. *M. tuberculosis* surveys, either by acid-fast staining or PCR, should be performed routinely in these patients.

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